

WHAT IS CLAIMED IS:

1. An expression vector for persistently maintaining expression of an tolerogenic epitope in an animal comprising:
  - (a) a DNA sequence coding for a fusion immunoglobulin operably linked to transcriptional and translational control regions functional in a hemopoietic cell or lymphoid cell, wherein the fusion immunoglobulin has at least one heterologous tolerogenic epitope at the N-terminus variable region; and wherein said DNA sequence is operably linked to
  - (b) a vector that can provide for stable maintenance of the DNA sequence in the hemopoietic cell or lymphoid cell.
2. An expression vector according to claim 1, wherein the vector is a retroviral vector.
3. An expression vector according to claim 1, wherein the DNA sequence codes for a fusion IgG having a heterologous tolerogenic epitope inserted adjacent to the first framework region of the N-terminus variable region of the heavy chain.
4. An expression vector according to claim 3, wherein the DNA sequence encodes a fusion IgG including an epitope having the amino acid sequence of amino acids 12-26 of the  $\lambda$  CI repressor protein.
5. An expression vector according to claim 1, wherein the transcriptional and translational control regions provide for constitutive expression of the DNA sequence in the lymphoid cells.

6. A method for tolerizing an animal to an epitope comprising:

(a) providing a vector that can be stably maintained in a hemopoietic or lymphoid cell, wherein the vector comprises a DNA sequence that codes for a fusion immunoglobulin operably linked to transcriptional and translational control regions functional in the hemopoietic or lymphoid cell, wherein the fusion immunoglobulin has at least one heterologous tolerogenic epitope at the N-terminus variable region;

(b) stably transforming a population of the hemopoietic or lymphoid cells from the animal with the vector to form a transformed population of hemopoietic or lymphoid cells expressing the fusion immunoglobulin; and

(c) introducing the transformed population of cells into an animal.

7. A method according to claim 6, wherein the fusion immunoglobulin has a tolerogenic epitope having the amino acid sequence of amino acids 12-26 of the  $\lambda$  CI repressor protein, wherein the tolerogenic epitope is inserted at the first framework region of the N-terminus of the variable heavy chain.

8. A method according to claim 7, wherein the vector is a retroviral vector.

9. A method according to claim 6, further comprising irradiating the animal sufficiently to destroy endogenous hemopoietic cells before introducing the transformed hemopoietic cells into the animal.

10. An expression cassette for expression of a DNA sequence in a hemopoietic or lymphoid cell comprising:
  - (a) a DNA sequence coding for a fusion immunoglobulin wherein the fusion immunoglobulin has at least one heterologous tolerogenic epitope inserted adjacent to the first framework region at the N-terminus of the variable region of the immunoglobulin, operably linked to transcriptional and translational control regions functional in the hemopoietic or lymphoid cells.
11. An expression cassette according to claim 10, wherein the epitope has the amino acid sequence of amino acids 12-26 of the  $\lambda$  CI repressor protein.
12. An expression cassette according to claim 11, wherein the fusion immunoglobulin is an IgG.
13. A plasmid having the characteristics of ATCC No. \_\_\_\_\_.
14. A pharmaceutical composition comprising:
  - (a) a tolerogenic amount of a fusion immunoglobulin, wherein the fusion immunoglobulin has at least one heterologous tolerogenic epitope adjacent to the first framework region of the N-terminus variable chain; and
  - (b) a pharmaceutically acceptable excipient.
15. A pharmaceutical composition according to claim 14, wherein the pharmaceutical immunoglobulin is an isologous IgG.

16. A pharmaceutical composition according to claim 15, wherein the fusion immunoglobulin has an heterologous tolerogenic epitope with an amino acid sequence of amino acids 12-26 of the  $\lambda$  CI repressor protein.
17. A pharmaceutical composition, wherein the excipient is selected from the group consisting of phosphate buffered saline, physiological saline and water.
18. A pharmaceutical composition, wherein the tolerogenic amount of the fusion immunoglobulin is about 4 to 40 mg/kg of body weight of the animal.
19. A transformed hemopoietic or lymphoid cell comprising an expression cassette stably maintained in the hemopoietic or lymphoid cell, wherein the expression cassette comprises a DNA sequence coding for a fusion immunoglobulin, wherein the fusion immunoglobulin has at least one heterologous tolerogenic epitope inserted adjacent to the first framework region at the N-terminal variable region, wherein said DNA sequence is operably linked to transcriptional and translational control regions functional in the hemopoietic or lymphoid cell.
20. A transformed cell according to claim 19, wherein the cell is a bone marrow cell.
21. A method for identifying tolerogenic epitopes comprising:
  - (a) providing a vector that can be stably maintained in a hemopoietic or lymphoid cell, wherein the vector comprises a DNA sequence that codes for a fusion immunoglobulin operably linked to transcriptional and translational control regions

functional in the hemopoietic or lymphoid cell, wherein the fusion immunoglobulin has at least one heterologous epitope at the N-terminus variable region;

(b) stably transforming a population of hemopoietic or lymphoid cells from an animal with the vector to form a population of transformed cells;

(c) introducing the transformed cells into an animal; and

(d) identifying whether the heterologous epitope is a novel tolerogen by determining whether the animals are tolerant to the heterologous epitope.

22. A method of identifying tolerogenic epitopes comprising;

(a) providing a vector that can be stably maintained in a host cell, wherein the vector comprises a DNA sequence that codes for a fusion immunoglobulin operably linked to transcriptional and translational control regions functional in the host cell, wherein the fusion immunoglobulin has at least one heterologous epitope at the N-terminus variable region of the immunoglobulin;

(b) stably transforming a population of host cells with the vector to form a population of transformed cells, producing the fusion immunoglobulins; and

(c) identifying whether the heterologous epitope on the fusion immunoglobulin is a tolerogenic epitope by determining whether the epitope is associated with an autoimmune or allergic immune response.

23. A method according to claim 22, wherein the host cell is E. coli.

24. A method according to claim 22, wherein the vector is a phagemid vector.
25. A method according to claim 22, wherein the host cell is a J558L cell.
26. A method according to claim 22, wherein the step of identifying whether the heterologous epitope on the fusion immunoglobulin is a tolerogen comprises:
- (a) determining whether the fusion immunoglobulin immunoreacts with immune serum from an autoimmune or allergic animal.
27. A method according to claim 22, wherein the step of identifying whether the heterologous epitope on the fusion immunoglobulin is a tolerogen comprises:
- (a) determining whether the fusion immunoglobulin stimulates proliferation of lymphocytes from an autoimmune or allergic animal.
28. A method according to claim 22 further comprising:
- (a) confirming that the heterologous epitope is a tolerogenic epitope by determining whether the fusion immunoglobulin induces tolerance to the epitope in an animal.
29. A method of tolerizing an animal to an epitope comprising: administering a fusion immunoglobulin having a heterologous tolerogenic epitope to an animal sufficiently to induce tolerance to the heterologous tolerogenic epitope, wherein the fusion immunoglobulin has the heterologous tolerogenic epitope at the first N-terminus framework region of the immunoglobulin.

30. A method of inducing and maintaining tolerance to an epitope in an animal comprising:
- (a) administering a pharmaceutical composition according to claim 14 sufficiently to induce tolerance to an epitope; and
  - (b) administering transformed hemopoietic or lymphoid cells to the animal sufficiently to maintain tolerance to the epitope, wherein the transformed cell comprises a vector stably maintained in the transformed cell, wherein the vector comprises a DNA sequence coding for a fusion immunoglobulin operably linked to transcriptional and translational control regions functional in the cell, wherein the fusion immunoglobulin has at least one heterologous tolerogenic epitope at the N-terminus variable region of the immunoglobulin.

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B<sup>1</sup> ✓

ADD  
E<sup>1</sup> ✓

add F<sup>4</sup> ✓

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G<sup>3</sup> ✓